

REMARKS

Applicants thank the Examiner for the thorough examination given the present application.

Status of the Claims

Claims 1, 3-11, 13-15, 17-22, and 24 are pending in the above-identified application. Claims 18-22 are currently withdrawn from consideration. Claims 1, 3-11, 13-15, 17, and 24 stand ready for further action on the merits. Claims 1 and 24 have been amended to correct a minor grammatical error. The amendments to claims 1 and 24 are non-narrowing. Thus, no new matter has been added. Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Priority Under 35 U.S.C. § 119

Applicants thank the Examiner for acknowledging Applicants' claim for foreign priority under 35 U.S.C. § 119 and receipt of the certified priority document.

Information Disclosure Citation

Applicants thank the Examiner for considering the references supplied with the Information Disclosure Statement filed September 30, 2009 and for providing Applicants with an initialed copy of the PTO-SB08 form filed therewith.

Drawings

Since no objection has been received, Applicant assumes that the drawings are acceptable and that no further action is necessary. Confirmation thereof in the next Office Action is respectfully requested.

Statement of the Substance of the Interview

Applicants thank the Examiner for the interview on April 9, 2010. Applicants appreciate the courtesies extended to Applicants' Representative in this application. In compliance with MPEP § 713.04, Applicants submit the following remarks.

The Interview Summary sufficiently summarizes the discussions during the interview. In addition, the Examiner agreed that some of the novel aspects of the present invention include the mixing of the drug-containing solution of a drug and a good solvent with a poor solvent and the lack of a pretreatment step. Also, the Examiner recommended conducting comparative testing wherein the comparative examples would either lack some feature of the mixing step or have a pretreatment step.

Based on the remarks below, Applicants believe that the claims are now in condition for allowance. Should the Examiner believe that there remains any outstanding issues, Applicants respectfully request that the Examiner contact Applicants' Representative so as to expedite resolution of these outstanding issues, via an Examiner's Amendment or the like.

Issues under 35 U.S.C. § 103(a)

Claims 1, 3-11, 13-15, 17, and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chaubal et al. '662 (US 2004/0245662) in view of Thumm et al. '332 (US

6,221,332). Applicants respectfully traverse. Reconsideration and withdrawal of the outstanding rejection are respectfully requested in view of the following considerations.

Legal Standard for Determining Prima Facie Obviousness

MPEP § 2141 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which has provided the controlling framework for an obviousness analysis. The four *Graham* factors are:

- (a) determining the scope and content of the prior art;
- (b) ascertaining the differences between the prior art and the claims in issue;
- (c) resolving the level of ordinary skill in the pertinent art; and
- (d) evaluating any evidence of secondary considerations.

Graham v. John Deere, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966).

Second, the Examiner has to provide some rationale for determining obviousness. MPEP § 2143 sets forth some rationales that were established in the recent decision of *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

As the MPEP directs, all claim limitations must be considered in view of the cited prior art in order to establish a *prima facie* case of obviousness. See MPEP § 2143.03.

Distinctions over the Cited References

Relevant to this § 103(a) rejection, one of the *Graham* factors is the evaluation of any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467. In this regard, Applicants respectfully submit that the present invention

has achieved unexpected results, whereby such results rebut any asserted *prima facie* case of obviousness and not yet has been properly been considered. *See In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Also, the comparative showing need not compare the claimed invention with all of the cited prior art, but only with the closest prior art. *See MPEP 716.02(b)* and *716.02(e)*.

Also, according to MPEP § 2145, rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995). Office personnel should consider all rebuttal arguments and evidence presented by Applicants. See, e.g., *Soni*, 54 F.3d at 750, 34 USPQ2d at 1687 (error not to consider evidence presented in the specification). Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *In re Dillon*, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990).

As stated above, the Examiner agreed that some of the novel aspects of the present invention include the mixing of the drug-containing solution of a drug and a good solvent with a poor solvent and the lack of a pretreatment step. Accordingly, the Examiner recommended conducting comparative testing wherein the comparative examples would either lack some feature of the mixing step or have a pretreatment step. Applicants note that the claims are directed to a process (versus, e.g., a product-by-process). Still, given the Examiner's request, Applicants submit the following explanation.

When comparing average particle size, Example 1 is unexpectedly superior over the comparative examples of the present specification. In fact, the comparative examples strongly evidence that the prior art does not produce the results of the present invention. Specifically,

Comparative Examples 1-3 show a pretreatment step, no good solvent, and high-pressure mixing. Comparative Example 4 uses no pretreatment step, no good solvent, and wet-homogenizing. Comparative Example 5 uses no pretreatment step, no good solvent, and a sonicator treatment. As shown in Table 1 on page 28 of the present specification and reproduced below, inventive Example 1 unexpectedly achieves better average particle size compared to these comparative examples. Applicants respectfully submit that this comparative testing meets the Examiner's suggestions during the interview.

	Preparation Method	Apparatus	Average particle size (nm)
Example 1	the present invention	Microfluidizer	218
Comparative Example 1	high-pressure emulsification	Microfluidizer	856
Comparative Example 2	high-pressure emulsification	piston-gap homogenizer	387
Comparative Example 3	high-pressure emulsification	Nanomizer	366
Comparative Example 4	wet pulverization	Dyno-Mill	465
Comparative Example 5	ultrasonication	sonicator	490

As stated in *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007): “rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” Furthermore, the mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *Id.*

As described above, Applicants have shown that the present invention achieves unexpected and unpredictable results. Thus, due to the unexpected results as achieved by the

present invention, the rejection has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez, Registration No. 48,501, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

Reply to Office Action of December 28, 2009

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

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